The Synthesis of 1,2,3-Triazoles from Nitroalkenes – Revisited

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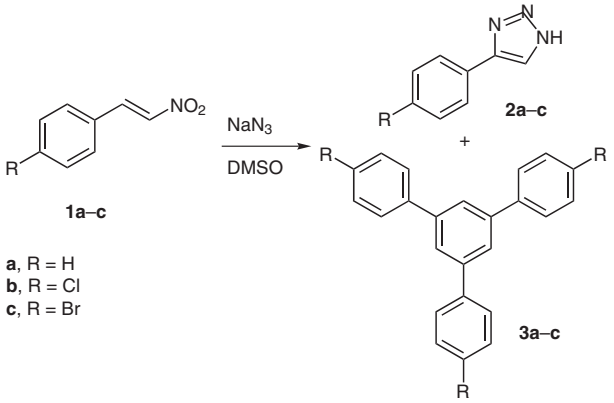
This paper is dedicated with respect and affection to Professor Steven V. Ley on the occasion of his 60th birthday.

Abstract: Nitroalkenes or vicinal acetoxy nitro derivatives undergo a clean reaction with sodium azide in hot dimethyl sulfoxide to give the corresponding 1,2,3-triazoles in good yield.

Key words: azides, cyclisations, heterocycles, nitroalkenes, 1,2,3-triazoles

In 1971, Zefirov et al.[1] reported that the reaction of sodium azide with nitrostyrenes **1a–c** led to the formation of the corresponding triazoles **2a–c** in about 60% yield as well as to 'considerable quantities' of 1,3,5-triarylbenzenes **3a–c** (Scheme 1).[2] The reactions were performed in dimethyl sulfoxide at room temperature and no other products were apparently isolated. Although a reasonable mechanism can be written for these transformations, we were intrigued by the fact that the action of an azide on a nitrostyrene could lead to a 1:1 ratio of both triazole **2** and trimer **3**, resulting from the ultimate interaction of three molecules of the nitrostyrene without the formation of major side products from the reaction of one or more of the intermediates with the azide anion. It seemed, therefore, worthwhile re-examining this intriguing transformation, more than thirty years after its discovery.



Scheme 1

Relying on the scant experimental information given in the communication, we exposed nitrostyrene **1a** to sodium azide (2 equiv) in dimethyl sulfoxide (1 mmol, 2 mL). The starting material disappeared within an hour, but only a small amount of triazole **2a** was isolated and no triphenylbenzene **3a** was formed, as indicated by comparison (TLC and HPLC) with an authentic sample. The major product turned out to be compound **9a** (determined by NMR and mass spectrometric analysis), logically derived by addition of azide to a molecule of nitrostyrene, followed by conjugate addition of the resulting nitronate **4a** to another molecule of nitrostyrene to give **7a** as outlined in Scheme 2. Equilibration with **8a** and ring closure involving elimination of nitrite, as shown for the transformation of **4a** into **2a** via **5a** and **6a**, finally provides the observed triazole **9a**. Various experimental modifications in terms of concentration and ratios of reactants, whilst keeping the medium at room temperature, did not significantly alter the results.

The NMR spectrum of the crude reaction mixture indicated the presence of other compounds, some of which could be obtained semi-pure by chromatography and whose spectra indicated structures of type **10a** and **11a**. These derivatives, which arise by addition of the triazoles to the starting nitrostyrene, were not thermally stable. Attempted recrystallisation caused partial decomposition via a retro-Michael reaction. Their exact structure could not, therefore, be determined unambiguously.

When we carried out the reaction at 80 °C, the outcome was very different. Both phenyltriazole **2a** and 1,3,5-triphenylbenzene (**3a**) were obtained in 24 and 13% yield, respectively, but triazole **9a** was nevertheless still produced, in approximately 40% yield. Heating resulted in a much cleaner reaction because side products such as **10a** and **11a** were automatically decomposed to release the nitrostyrene, which could then react with the azide anion. How Zefirov and his co-workers obtained phenyltriazole **2a** and triphenylbenzene **3a** by operating at room temperature and at the same time did not observe any significant amount of triazole **9a**, nor compounds of type **10a** and **11a**, remains an inexplicable mystery. This is all the more surprising because the formation of both **3a** and **9a** proceeds by way of intermediate **7a** and possibly also via **8a**, depending on whether the addition of the third nitrostyrene molecule precedes or follows the elimination of the azide anion. Moreover, the formation of triphenylbenzene is a more complex process that is slower than the one leading to triazole **9a**, which occurs readily even at room temperature. It must be said that the manifold reaction displayed in Scheme 2 only highlights what we feel are the main pathways, but remains nevertheless incomplete

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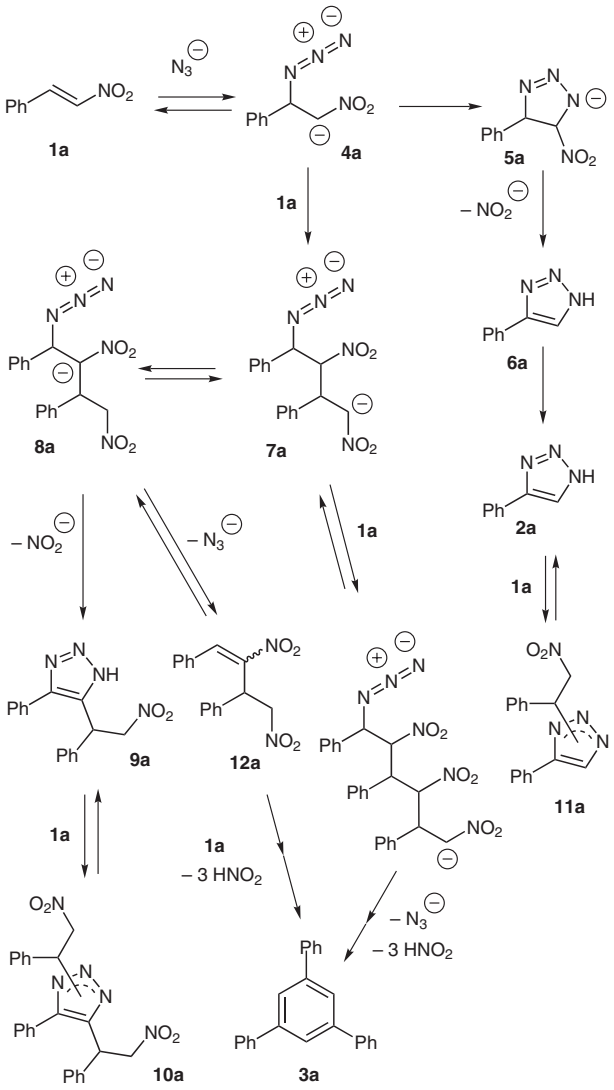
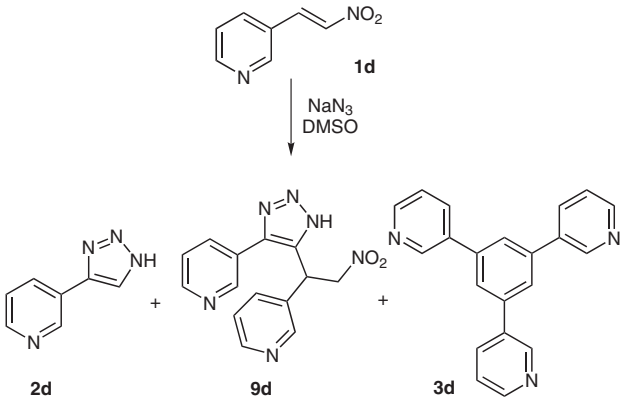


Scheme 2

despite its complexity. Various alternative routes and possible side reactions have been omitted for clarity.

We performed an analogous series of experiments starting from 3-(2-nitrovinyl)pyridine (**1d**). The qualitative outcome was similar, even if the reactions were faster due to the greater electrophilicity of **1d** compared to nitrostyrene (Scheme 3). Furthermore, the pyridine series proved easier to analyse because of the greater spread of the signals in the NMR spectra. Thus, reaction at room temperature produced mostly triazole **9d**, but this time triazole **2d** and trimer **3d** could also be observed; at 80 °C, a separable mixture of **2d**, **3d**, and **9d** was obtained (25, 15, and 17% yield, respectively).



Scheme 3

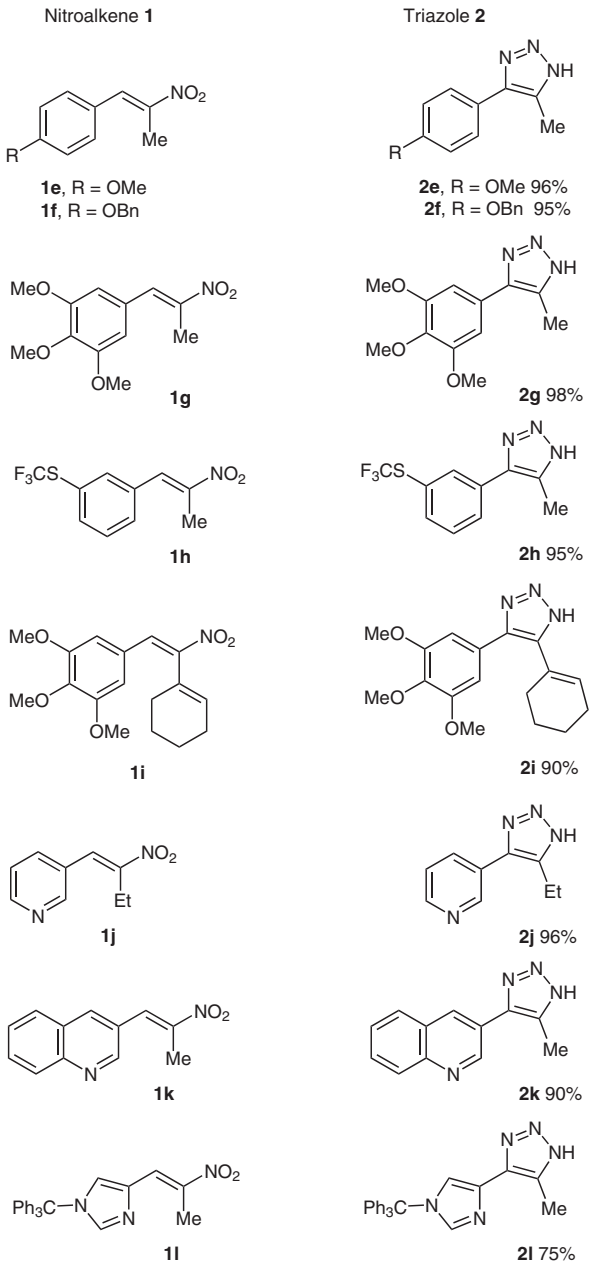


Figure 1 Formation of 1,2,3-triazoles from nitroalkenes

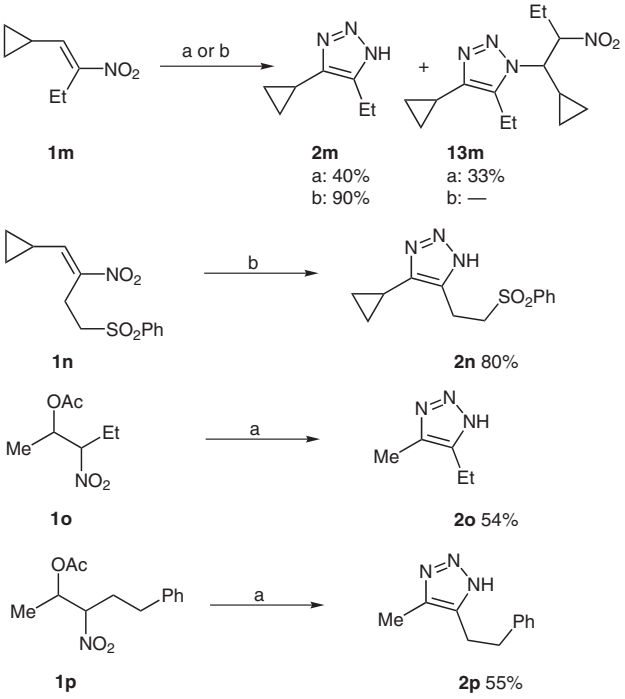
The above experiments provided us with a better mechanistic picture and gave us a feel for the rates of the various steps. In particular, it became apparent that ring closure leading to the tetrazole of a primary nitronate, such as **4a**, is in fact a sluggish process at room temperature and the intermolecular Michael addition to a nitroalkene molecule is preferred. This suggested a simple modification of the

experimental procedure that would suppress the unwanted side reactions. Because the ring closure is by definition unimolecular and, therefore, insensitive to concentration, slow addition of the nitroalkene to a hot solution of sodium azide in dimethyl sulfide should favour the formation of the desired triazole **2** relative to the other products, which all derive from further bimolecular reactions with the nitroalkene. Indeed, under these conditions, the yields of triazoles **2a** and **2d** increased to 78 and 80%, respectively, and only very small amounts of the other products were observed in the NMR spectra of the crude reaction mixtures.

The reaction now becomes a synthetically useful route to 1,2,3-triazoles. Furthermore, the ease of formation of compound **9a** (or **9d**), even at room temperature, indicated that ring closure of a secondary nitronate is, contrastingly, a quite facile process. In fact, with nitroalkenes possessing a substituent geminal to the nitro group, there was no need for slow addition. Mixing all the ingredients [nitroalkene **1** (1 mmol), NaN_3 (2 mmol), DMSO (2 mL)] and heating at 80–90 °C for a few hours brought about the desired transformation in generally high yield, as indicated by the results compiled in Figure 1. In most cases, triazole **2** could be recovered by simple filtration after dilution of the reaction mixture with water, and purified by recrystallisation. The starting nitroalkenes are readily obtained by condensation of the appropriate nitroalkane with the desired aromatic or heteroaromatic aldehyde.[3]

When we examined the reaction of nitroalkene **1m**, derived from cyclopropanecarbaldehyde, with sodium azide, we were surprised to find that under otherwise identical conditions of temperature and dilution to those above, compound **13m** was formed in 33% yield, in addition to the expected triazole **2m** (40% yield; Scheme 4). Compound **13m** arises from the Michael addition of triazole **2m** to the starting nitroalkene **1m**, a transformation that appears to be especially facile in this case. The formation of this unwanted side product could be suppressed by doubling the volume of dimethyl sulfoxide and the quantity of sodium azide. Under these modified conditions, the yield of triazole **2m** increased to 90%. With the more hindered nitroalkene **1n**, no complications from subsequent conjugate addition of the product were observed and the reaction proceeded normally to furnish triazole **2n** in 80% yield.

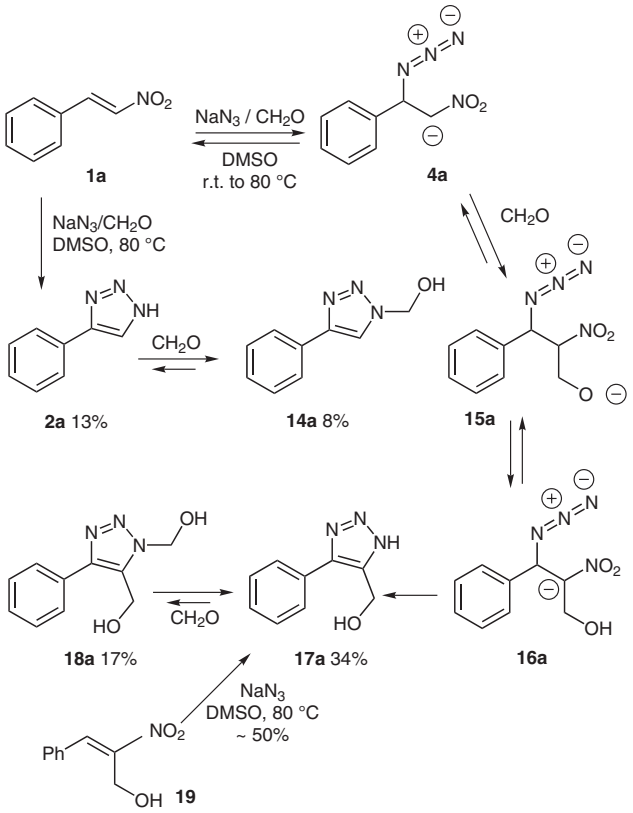
In the case of purely aliphatic derivatives, it was more convenient to start directly from the vicinal acetoxy nitro precursors, which are easily prepared by the Henry addition of a nitroalkane to an aldehyde, followed by acetylation of the nitro alcohol.[3] The mild basic character of the sodium azide is sufficient to induce the β-elimination of the acetoxy group and produce the nitroalkene in situ. Thus, the vicinal acetoxy nitro derivative acts as a convenient surrogate for the somewhat delicate nitroalkene. In this manner, 2-acetoxy-3-nitropentane **1o** and 2-acetoxy-3-nitro-5-phenylpentane **1p** could be converted into triazoles **2o** and **2p** in 54 and 55% yield, respectively, as depicted in Scheme 4.



Scheme 4 *Reagents and conditions*: (a) nitroalkene (1 mmol), NaN_3 (2 mmol), DMSO (1.2 mL), 80–90 °C; (b) nitroalkene (1 mmol), NaN_3 (4 mmol), DMSO (4 mL), 80–90 °C.

Finally, we examined the possibility of constructing the triazoles through a multicomponent process as outlined in Scheme 5. The concept hinges on the possibility of capturing the initial azide adduct **4a** with formaldehyde before ring closure to the triazole occurs. Indeed, heating nitrostyrene **1a** with sodium azide and aqueous formaldehyde produced the expected hydroxymethyl-substituted triazole **17a**, albeit in modest yield (34%). However, premature closure to the simple triazole **2a** (13%) and, more importantly, to N-hydroxymethylated derivatives **14a** (8%) and **18a** (17%) could not be avoided. Heating the crude residue in refluxing methanolic sodium hydroxide caused the elimination of formaldehyde from compounds **14a** and **18a** and resulted in an increase in the yield of **17a** to 47%. The structure of **17a** was confirmed by an alternative synthesis from preformed 2-nitro-3-phenylprop-2-enol (**19**). Despite its lack of efficiency at this stage, this approach provides, nevertheless, an expedient entry into hydroxymethyl-substituted triazoles. These are rare compounds[4] and may prove to be useful starting materials for the synthesis of more complex triazoles by substitution or modification of the alcohol function.

In summary, while attempting to understand the observations of Zefirov and co-workers, we developed a practical and efficient access to 1,2,3-triazoles. This family of compounds has been recently popularised by Sharpless through what is now called 'click' chemistry[5] and several members of it are reported to have interesting pharmacological properties.[6] It is noteworthy that simple 4-aryl-1,2,3-triazoles (e.g., **2a**, **2d**) were very recently found to be potent, nanomolar inhibitors of angiogenesis in vivo.[7]



Scheme 5 A three-component synthesis of hydroxymethyl triazoles

Solvents were used as received. Merck Geduran SI 60 Å silica gel (35–70 μm) was used for column chromatography. Petroleum ether used had the boiling range 40–60 °C. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded using 400 MHz ARX 400 Brucker spectrometers. Chemical shifts are given in ppm, referenced to the residual proton resonances of the solvents. Nitrostyrene is commercially available; nitroalkenes **1d**,[8] **1e**,[9] **1f**,[10] **1g**,[11] **1i**,[12] and **1l**[13] and nitroacetates **1o**[14] and **1p**[15] were prepared according to literature procedures. Compound **1h** was a gift from Synthelabo (now Sanofi-Aventis).

Nitroalkenes 1j, 1k, and 1m; General Procedure

A solution of the aldehyde (20 mmol) in the requisite nitroalkane (20 mL) was heated at 100 °C in the presence of ethylenediamine (0.44 mL).[16] The mixture was cooled and the precipitate filtered and dried in the case of solid nitroalkenes. Otherwise, the solvent was evaporated and the residue was purified by flash column chromatography (silica gel).

3-[(*E*)-2-Nitrobut-1-enyl]pyridine (1j)

This compound was prepared from pyridine-3-carbaldehyde and 1-nitropropane, and was isolated as a yellow oil after chromatography (silica gel, PE–EtOAc 7:3).

Yield: 1.2 g (34%).

IR (CCl_4): 1659, 1559, 1531 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.67 (d, 1 H, *J* = 2.1 Hz, C*H*Ar), 8.64 (dd, 1 H, *J* = 1.4, 4.8 Hz, C*H*Ar), 7.94 (s, 1 H, C*H*), 7.72 (dt, 1 H, *J* = 1.6, 7.9 Hz), 7.40 (dd, 1 H, *J* = 4.8, 7.9 Hz), 2.84 (q, 2 H, *J* = 7.4 Hz), 1.27 (t, 3 H, *J* = 7.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9 (*C*q), 150.7, 150.3, 136.4, 129.3 (*C*H), 128.6 (*C*q), 123.7 (*C*H), 20.9 (CH_2), 12.6 (CH_3).

MS (CI, NH_3): *m*/*z* = 179 [M + H$^+$].

3-[(*E*)-2-Nitropropenyl]quinoline (1k)

This compound was prepared from quinoline-3-carbaldehyde (1 g, 6.37 mmol) and nitroethane (1 mL), and was isolated as crystals after chromatography (silica gel, toluene–EtOAc 95:5).

Yield: 0.81 g (60%)

Mp 96–97 °C (EtOAc–PE).

IR (CCl_4): 1656, 1614, 1567, 1518, 1503 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.96 (s, 1 H, N=C*H*), 8.23 (s, 2 H, C*H*), 8.14 (d, 1 H, *J* = 8.3 Hz, C*H*), 7.89 (d, 1 H, *J* = 8.2 Hz, C*H*), 7.82 (t, 1 H, *J* = 7.8 Hz, C*H*), 7.64 (t, 1 H, *J* = 8.0 Hz, C*H*), 2.56 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.6 (*C*H), 149.1, 148.0 (*C*q), 137.2, 131.2, 130.1, 129.5, 128.3, 127.8 (*C*H), 127.3, 125.7 (*C*q), 14.3 (CH_3).

MS (CI, NH_3): *m*/*z* = 215 [M + H$^+$].

Anal. Calcd for $C_{12}H_{10}N_2O_2$: C, 67.28; H, 4.71. Found: C, 67.08; H, 4.59.

[(*E*)-2-Nitrobut-1-enyl]cyclopropane (1m)

This compound was prepared from cyclopropanecarbaldehyde and 1-nitropropane, and was isolated as a yellow oil after chromatography (silica gel, PE–Et_2O, 95:5).

Yield: 2.06 g (73%).

IR (CCl_4): 1661, 1522 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.52 (d, 1 H, *J* = 11.1 Hz, C*H*=C), 2.70 (q, 2 H, *J* = 7.4 Hz, CH_2CH_3), 1.57 (m, 1 H, C*H*), 1.17 (t, 3 H, *J* = 7.4 Hz, CH_2CH_3), 1.11 (m, 2 H, CH_2), 0.77 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1 (*C*q), 142.1 (*C*H=C), 20.1 (CH_3), 12.6 (CH_2), 11.0 (2 CH_2), 9.2 (*C*H).

MS (CI, NH_3): *m*/*z* = 159 [M + H$^+$ + NH_3].

{[(*E*)-4-Cyclopropyl-3-nitrobut-3-enyl]sulfonyl}benzene (1n)

A mixture of 3-(phenylsulfonyl)-1-nitropropane[17] (0.16 g, 0.69 mmol) and cyclopropanecarbaldehyde (0.073 g, 1.04 mmol) was stirred at r.t. overnight in the presence of DMAP (10 mg, 0.08 mmol). The mixture was diluted with THF (0.5 mL) and treated with Ac_2O (0.2 mL). The reaction was quenched with MeOH and the solvent was evaporated off under reduced pressure. The residue was purified by chromatography (silica gel, toluene–EtOAc 95:5) to yield **1n** as crystals.

Yield: 0.1 g (50%).

Mp 106–107 °C (Et_2O–PE).

IR (CCl_4): 1659, 1521, 1327, 1156, 1142 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, 2 H, *J* = 7.2 Hz, C*H*Ar), 7.69 (t, 1 H, *J* = 7.4 Hz, C*H*Ar), 7.60 (t, 2 H, *J* = 7.6 Hz, C*H*Ar), 6.64 (d, 1 H, *J* = 11.3 Hz, C*H*=C), 3.39 (dd, 2 H, *J* = 6.4, 8.9 Hz, CH_2), 3.14 (dd, 2 H, *J* = 6.4, 9.0 Hz, CH_2), 1.60 (m, 1 H, CH), 1.20 (m, 2 H, CH_2), 0.83 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.3 (*C*H), 145.0, 138.6 (*C*q), 134.0, 129.4, 127.9 (*C*H), 53.5 (CH_2SO_2), 20.6 (CH_2), 11.6 (*C*H), 10.1 (2 CH_2).

MS (CI, NH_3): *m*/*z* = 282 [M + H$^+$], 299 [M + H$^+$ + NH_3].

1,2,3-Triazoles 2; General Procedure

To a solution of the nitroalkene (1 mmol) in DMSO (2 mL) was added NaN_3 (2 mmol). The mixture was then heated at 80–90 °C until the starting material was totally consumed as indicated by TLC (30 min to 8 h). After cooling, H_2O was added and the resulting pre-

cipitate was filtered, washed with H_2O, and dried to give the desired triazole, which was recrystallised. When no precipitate was observed, the triazole was isolated after extraction with EtOAc or Et_2O.

4-(4-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazole (2e)
This compound was isolated as white crystals.

Yield: 0.364 g (96%).

Mp 169–170 °C (EtOAc–PE).

^{1}H NMR (400 MHz, $CDCl_3$–CD_3OD): δ = 7.61 (d, 2 H, *J* = 8 Hz, C*H*Ar), 6.98 (d, 2 H, *J* = 8 Hz, C*H*Ar), 3.84 (s, 3 H, OCH_3), 2.49 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$–CD_3OD): δ = 159.4 (*C*q, *C*OMe), 128.4 (2 *C*HAr), 123.3 (*C*q), 114.3 (2 *C*HAr), 55.3 (O*C*H$_3$), 10.9 (*C*H$_3$).

MS (CI, NH_3): *m*/*z* = 190 [M + H$^+$].

HMRS (EI): *m*/*z* [M$^+$] calcd for $C_{10}H_{11}N_3O$: 189.0902; found: 189.0901.

4-(4-Benzyloxyphenyl)-5-methyl-1*H*-1,2,3-triazole (2f)
This compound was isolated as white crystals.

Yield: 0.505 g (95%).

Mp 166–169 °C (EtOAc–PE).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, 2 H, *J* = 8.7 Hz), 7.46–7.30 (m, 5 H, C*H*Ar), 7.06 (d, 2 H, *J* = 8.8 Hz, C*H*Ar), 5.10 (s, 2 H, OCH_2Ph), 2.48 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$–CD_3OD): δ = 158.4, 136.5 (*C*q, Ar), 128.4, 128.2, 127.9, 127.3 (*C*HAr), 123.0 (*C*q), 114.9 (*C*HAr), 69.9 (*C*H$_2$Ph), 10.5 (*C*H$_3$).

MS (CI, NH_3): *m*/*z* = 266 [M + H$^+$].

Anal. Calcd for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70. Found: C, 72.51; H, 5.54.

5-Methyl-4-(3,4,5-trimethoxyphenyl)-1*H*-1,2,3-triazole (2g)
This compound was isolated as white crystals.

Yield: 0.43 g (98%).

Mp 124–125 °C (EtOAc–PE).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94 (s, 2 H, C*H*), 3.92 (s, 6 H, 2 OCH_3), 3.90 (s, 3 H, OCH_3), 2.55 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.3 (*C*q, 3 *C*OMe), 137.7, 126.3 (*C*q), 104.3 (2 *C*HAr), 60.9 (O*C*H$_3$), 56.1 (2 O*C*H$_3$), 10.9 (*C*H$_3$).

MS (CI, NH_3): *m*/*z* = 250 [M + H$^+$], 267 [M + H$^+$ + NH_3].

Anal. Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.07. Found: C, 57.92, H, 6.09.

5-Methyl-4-{3-[(trifluoromethyl)sulfanyl]phenyl}-1*H*-1,2,3-triazole (2h)
This compound was isolated as white crystals.

Yield: 0.492 g (95%).

Mp 116–117 °C (CH_2Cl_2–PE).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (s, 1 H, C*H*), 7.86 (d, 1 H, *J* = 8 Hz, C*H*), 7.67 (d, 1 H, *J* = 8 Hz, C*H*), 7.52 (t, 1 H, *J* = 8 Hz, C*H*), 2.57 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.6, 134.6 (*C*H), 129.5 (q, *J* = 306 Hz, S*C*F$_3$), 132.2 (*C*q), 129.9, 129.4 (*C*HAr), 125.0 (*C*q), 10.8 (*C*H$_3$).

MS (CI, NH_3): *m*/*z* = 260 [M + H$^+$].

Anal. Calcd for $C_{10}H_8F_3N_3S$: C, 46.33; H, 3.11. Found: C, 46.61; H, 3.02.

5-Cyclohex-1-enyl-4-(3,4,5-trimethoxyphenyl)-1*H*-1,2,3-triazole (2i)
This compound was isolated as a yellow oil after chromatography (silica gel, EtOAc–PE 1:1).

Yield: 0.285 g (90%).

IR (CCl_4): 3454, 3149 cm^{-1} (NH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (s, 2 H, C*H*Ar), 6.10 (m, 1 H, C=C*H*), 3.89 (s, 3 H, OCH_3), 3.85 (s, 6 H, 2 OCH_3), 2.32 (m, 2 H), 2.13 (m, 2 H, CH_2), 1.73 (m, 2 H, CH_2), 1.65 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.1 (*C*q, 3 *C*OCH$_3$), 137.6 (*C*q), 130.5 (*C*H=C), 127.5, 126.5 (*C*q,), 104.7 (2 *C*HAr), 60.9 (O*C*H$_3$), 55.9 (2 O*C*H$_3$), 27.5, 25.5, 22.6, 21.7 (*C*H$_2$).

MS (CI, NH_3): *m*/*z* = 316 [M + H$^+$].

HRMS (EI): *m*/*z* [M$^+$] calcd for $C_{17}H_{21}N_3O_3$: 315.1583; found: 315.1584.

3-(5-Ethyl-1*H*-1,2,3-triazol-4-yl)pyridine (2j)
After extraction with Et_2O, the compound was isolated as white crystals.

Yield: 0.334 g (96%).

Mp 115–116 °C (Et_2O–PE).

^{1}H NMR (400 MHz, $CDCl_3$–CD_3OD): δ = 8.95 (d, 1 H, *J* = 1.5 Hz, C*H*Ar), 8.60 (dd, 1 H, *J* = 1.6, 4.9 Hz, C*H*Ar), 8.06 (dt, 1 H, *J* = 8.0, 1.6 Hz, C*H*Ar), 7.41 (ddd, 1 H, *J* = 0.8, 4.9, 7.9 Hz, *CH*Ar), 2.92 (q, 2 H, *J* = 7.6 Hz, CH_2CH$_3$), 1.33 (t, 3 H, *J* = 7.6 Hz, CH$_2$CH_3).

^{13}C NMR (100 MHz, $CDCl_3$–CD_3OD): δ = 148.3, 147.6 (*C*HAr), 140.1 (m, *C*q), 135.1 (*C*HAr), 127.8 (*C*q), 123.8 (*C*HAr), 18.5 (*C*H$_2$), 13.2 (*C*H$_3$).

MS (CI, NH_3): *m*/*z* = 175 [M + H$^+$].

Anal. Calcd for $C_9H_{10}N_4$: C, 62.05; H, 5.79. Found: C, 61.91; H, 5.84.

3-(5-Methyl-1*H*-1,2,3-triazol-4-yl)quinoline (2k)
This compound was isolated as a solid.

Yield: 0.376 g (90%).

Mp 229–230 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.36 (s, 1 H, C*H*=N), 8.67 (s, 1 H, C*H*Ar), 8.12 (d, 1 H, *J* = 7.6 Hz, C*H*Ar), 8.09 (d, 1 H, *J* = 8.4 Hz, C*H*Ar), 7.81 (t, 1 H, *J* = 7.6 Hz, C*H*Ar), 7.68 (t, 1 H, *J* = 7.6 Hz), 2.62 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 148.9 (*C*H=N), 146.6 (*C*q), 132.3, 129.6, 128.7, 128.3, 127.1 (*C*HAr), 127.4, 124.5 (*C*q).

MS (CI, NH_3): *m*/*z* = 211 [M + H$^+$].

HMRS (EI): *m*/*z* [M$^+$] calcd for $C_{12}H_{10}N_4$: 210.0905; found: 210.0910.

5-Methyl-4-(1-trityl-1*H*-imidazol-4-yl)-1*H*-1,2,3-triazole (2l)
This compound was isolated as a solid after chromatography (silica gel, EtOAc–PE 3:7).

Yield: 0.22 g (75%).

Mp 211–212 °C (DMSO).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (br s, 1 H, N*H*), 7.36 (m, 10 H, C*H*), 7.19 (m, 7 H, C*H*), 2.40 (br s, 3 H, CH_3).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 142.0 (*C*q), 138.7 (m, *C*q), 129.1, 128.3, 128.0 (*C*H), 74.8 (*C*q).

Anal. Calcd for $C_{25}H_{21}N_5$: C, 76.70; H, 5.41. Found: C, 76.52; H, 5.44.

4-Cyclopropyl-5-ethyl-1*H*-1,2,3-triazole (2m)

This compound was isolated in 40% yield using the general procedure described above, or using the modified procedure as follows: Nitroalkene **1m** (0.282 g, 2 mmol) was dissolved in DMSO (8 mL) and NaN_3 (0.52 g, 8 mmol) was added. After heating for 8 h at 80–90 °C, the mixture was cooled and extracted (Et_2O, 3×) to afford triazole **2m** as white crystals.

Yield: 0.247 g (90%).

Mp 110–111 °C (Et_2O–PE).

IR (CCl_4): 3466, 3170 cm^{-1} (NH).

^1H NMR (400 MHz, $CDCl_3$): δ = 13.6 (br s, 1 H, N*H*), 2.77 (q, 2 H, *J* = 7.6 Hz, CH_2CH$_3$), 1.80 (m, 1 H, C*H*), 1.30 (t, 3 H, *J* = 7.6 Hz, CH$_2$CH_3), 0.94 (m, 2 H, CH_2), 0.88 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8–145.2 (m, *C*q), 17.8 (*C*H$_3$), 13.4 (*C*H$_2$), 7.0 (2 *C*H$_2$), 5.3 (*C*H).

MS (CI, NH_3): *m*/*z* = 138 [M + H$^+$], 155 [M + H$^+$ + NH_3].

Anal. Calcd for $C_7H_{11}N_3$: C, 61.29; H, 8.08. Found: C, 61.44; H, 8.09.

4-Cyclopropyl-1-(1-cyclopropyl-2-nitrobutyl)-5-ethyl-1*H*-1,2,3-triazole (13m)

This compound was isolated as a solid as mixture of two diastereomers in a 2:1 ratio.

Yield: 0.093 g (33%).

Major isomer

IR (CCl_4): 1556 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.20 (dt, 1 H, *J* = 3.4, 10.4 Hz, C*H*NO$_2$), 4.22 (t, 1 H, *J* = 9.8 Hz, C*H*CHNO$_2$), 2.66 (q, 2 H, *J* = 7.6 Hz, CH_2CH$_3$), 2.26 (dqd, 1 H, *J* = 3.5, 7.5, 14.9 Hz, C*H*HCH$_3$), 2.05 (qdd, 1 H, *J* = 7.2, 10.9, 14.4 Hz, CH*H*CH$_3$), 1.71 (qd, 1 H, *J* = 5.0, 8.4 Hz, C*H*), 1.35–1.26 (m, 1 H, C*H*), 1.24 (t, 3 H, *J* = 7.6 Hz, CH$_2$CH_3), 1.02 (t, 3 H, *J* = 7.4 Hz, CH$_2$CH_3), 0.90–0.73 (m, 5 H, C*H*H, 2 CH_2), 0.52–0.37 (m, 3 H, CH*H*, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.8, 147.2 (*C*q), 92.6, 70.3 (*C*H), 24.3, 18.2 (*C*H$_2$), 13.5, 13.2 (*C*H$_3$), 10.3 (CH), 7.5, 7.3, 6.1 (*C*H$_2$), 5.7 (CH), 2.5 (*C*H$_2$).

MS (CI, NH_3): *m*/*z* = 279 [M + H$^+$], 296 [M + H$^+$ + NH_3].

Minor isomer

IR (CCl_4): 1556 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.01 (dt, 1 H, *J* = 3.1, 10.4 Hz, C*H*NO$_2$), 4.02 (t, 1 H, *J* = 9.8 Hz, C*H*CHNO$_2$), 2.70 (q, 2 H, *J* = 7.6 Hz, CH_2CH$_3$), 1.89–1.79 (m, 1 H, C*H*HCH$_3$), 1.78–1.71 (m, 1 H, CH*H*CH$_3$), 1.48–1.40 (m, 1 H, C*H*), 1.27 (t, 3 H, *J* = 7.6 Hz, CH$_2$CH_3), 1.20–1.10 (m, 1 H, C*H*), 0.96–0.91 (m, 2 H, CH_2), 0.84 (t, 3 H, *J* = 7.6 Hz, CH$_2$CH_3), 0.84–0.79 (m, 2 H, CH_2), 0.71–0.65 (m, 1 H, C*H*H), 0.46–0.41 (m, 1 H, CH*H*), 0.36–0.27 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.1, 147.5 (*C*q), 92.6, 70.2 (*C*H), 24.3, 18.3 (*C*H$_2$), 13.7, 13.6 (*C*H$_3$), 10.0 (*C*H), 7.5 (*C*H$_2$), 5.7 (*C*H), 5.6, 2.1 (*C*H$_2$).

MS (CI, NH_3): *m*/*z* = 279 [M + H$^+$], 296 [M + H$^+$ + NH_3].

5-[2-(Phenylsulfonyl)ethyl]-4-cyclopropyl-1*H*-1,2,3-triazole (2n)

This compound was prepared according to the modified procedure described for **2m** and was isolated as a foam after extraction with Et_2O.

Yield: 0.054 g (80%).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, 2 H, *J* = 8.1 Hz, C*H*Ar), 7.67 (t, 1 H, *J* = 7.4 Hz, C*H*Ar), 7.57 (t, 2 H, *J* = 7.7 Hz, C*H*Ar), 3.55 (m, 2 H, CH_2), 3.16 (m, 2 H, CH_2), 1.7 (m, 1 H, C*H*), 0.95 (m, 2 H, CH_2CH), 0.80 (m, 2 H, CH_2CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4, 140.8, 138.6 (*C*q), 133.8, 129.3, 128.0 (*C*H), 54.5, 18.2 (*C*H$_2$), 7.8 (2 *C*H$_2$), 5.5 (*C*H).

MS (CI, NH_3): *m*/*z* = 278 [M + H$^+$].

HMRS (EI): *m*/*z* [M$^+$] calcd for $C_{13}H_{15}N_3O_2S$: 277.0885; found: 277.0886.

5-Ethyl-4-methyl-1*H*-1,2,3-triazole (2o)

This known compound[18] was prepared from nitro acetate derivative **1o** (0.50 g, 2.85 mmol) in DMSO (3 mL) and obtained as an oil.

Yield: 0.17 g (54%).

^1H NMR (400 MHz, $CDCl_3$): δ = 2.68 (q, 2 H, *J* = 7.6 Hz, CH_2), 2.29 (s, 3 H, CH_3), 1.27 (t, 3 H, *J* = 7.6 Hz, CH_3).

MS (CI, NH_3): *m*/*z* = 112 [M + H$^+$].

4-Methyl-5-(2-phenylethyl)-1*H*-1,2,3-triazole (2p)

This compound was prepared according to the general procedure from nitro acetate **1p** and was isolated as crystals after extraction with Et_2O and chromatography (silica gel, PE–EtOAc 9:1 → 7:3).

Yield: 0.207 g (55%).

Mp 104–105 °C (Et_2O–PE).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.14 (m, 5 H, Ph), 2.97 (s, 4 H, 2 CH_2), 2.11 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.3, 141.0, 139.5 (*C*q), 128.4, 128.3, 126.1 (*C*HAr), 35.4 (Ar*C*H$_2$), 26.4 (*C*H$_2$), 9.1 (*C*H$_3$).

MS (CI, NH_3): *m*/*z* = 188 [M + H$^+$].

Anal. Calcd for $C_{11}H_{13}N_3$: C, 70.56; H, 7.00. Found: C, 70.53; H, 7.11.

1,2,3-Triazoles 14a, 17a, and 18a; Typical Procedure

To a solution of nitrostyrene (**1a**) (0.3 g, 2 mmol) in DMSO (5 mL) and aq CH_2O (20 mmol) was added portionwise NaN_3 (0.65 g, 10 mmol). The mixture was stirred for 1 h at r.t. and then heated at 80–90 °C for another 1 h. The solvent was removed by flushing with N_2 and the residue was taken up in a mixture of EtOAc and MeOH. After filtration and evaporation under reduced pressure, the residue was purified by chromatography (silica gel, PE–EtOAc gradient) and crystallisation to yield **14a** (0.029 g, 8%), **17a** (0.119 g, 34%), **18a** (0.069 g, 17%), and **2a** (0.038 g, 13%). When the crude mixture was refluxed in MeOH (5 mL) in the presence of NaOH (3 equiv) for 2 h, **17a** was obtained in 47% yield.

(4-Phenyl-1*H*-1,2,3-triazol-1-yl)methanol (14a)

This compound was isolated as a white solid.

Mp 100–101 °C (CH_2Cl_2–PE).

^1H NMR (400 MHz, $CDCl_3$–D_2O): δ = 7.91 (s, 1 H, C*H*=C), 7.77 (d, 2 H, *J* = 7.2 Hz, C*H*Ar), 7.43 (t, 2 H, *J* = 7.5 Hz, C*H*Ar), 7.37 (t, 1 H, *J* = 7.5 Hz, C*H*Ar), 5.81 (s, 2 H, CH_2OH).

^{13}C NMR (100 MHz, $CDCl_3$–D_2O): δ = 148.8 (*C*q), 132.2, 132.1, 129.8, 129.0, 128.9, 126.2, 126.1 (*C*q, *C*H), 76.3 (*C*H$_2$OH).

MS (CI, NH_3): *m*/*z* = 146 [MH – $CH_2O$$^+$], 176 [M + H$^+$].

Anal. Calcd for $C_9H_9N_3O$: C, 61.70; H, 5.18. Found: C, 61.65; H, 5.14.

(5-Phenyl-3*H*-1,2,3-triazol-4-yl)methanol (17a)

This compound was isolated as a white solid.

Mp 130–131 °C (CH_2Cl_2–MeOH).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 15.2 (br s, 1 H, N*H*), 8.01 (d, 2 H, *J* = 6.7 Hz), 7.66 (t, 2 H, *J* = 6.5 Hz), 7.56 (t, 1 H, *J* = 6.9 Hz), 5.65 (br s, 1 H, O*H*), 4.83 (s, 2 H, CH_2OH).

MS (CI, NH_3): *m*/*z* = 176 [M + H$^+$], 193 [M + H$^+$ + NH_3].

HMRS (EI): *m*/*z* [M$^+$] calcd for $C_9H_9N_3O$: 175.0745; found: 175.0744.

[5-(Hydroxymethyl)-4-phenyl-1*H*-1,2,3-triazol-1-yl]methanol (18a)

This compound was isolated as a white solid.

Mp 83–85 °C (CH_2Cl_2–PE).

^{1}H NMR (400 MHz, $CDCl_3$–D_2O): δ = 7.66 (d, 2 H, *J* = 7.3 Hz, C*H*Ar), 7.36 (m, 3 H, C*H*Ar), 5.71 (s, 2 H, NCH_2), 4.77 (s, 2 H, CH_2).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 145.3, 144.9, 130.4 (*C*q), 128.7, 128.2, 127.1 (*C*HAr), 75.9 (*C*H_2OH), 54.3 (*C*H_2OH).

MS (CI, NH_3): *m*/*z* = 176 [MH – CHO$^+$].

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40. Found: C, 58.42; H, 5.41.

Improved Synthesis of 1,2,3-Triazoles 2a and 2d

A solution of nitrostyrene (**1a**) (0.15 g, 1 mmol) in DMSO (7 mL) was added dropwise over 4 h to a hot (80–90 °C) solution of NaN_3 (0.13 g, 2 mmol) in DMSO (2 mL). The mixture was cooled and partitioned between H_2O and EtOAc, and the organic layer further washed with H_2O and dried (Na_2SO_4). Concentration under reduced pressure and purification of the residue by chromatography (silica gel, toluene–EtOAc 8:2) gave phenyltriazole **2a**; yield: 0.113 g (78%).

It was identical to an authentic sample.

The preparation of **2d** was carried out on a larger scale: Nitroalkene **1d** (1.00 g, 6.66 mmol) in DMSO (50 mL) was added dropwise over 4 h to a hot (80–90 °C) solution of NaN_3 (0.866 g, 13.5 mmol) in DMSO (13 mL). The mixture was worked up as for **2a**, but chromatographic purification was not necessary in this case.

3-(1*H*-1,2,3-triazol-4-yl)pyridine (2d)

This compound was isolated as a solid.

Yield: 0.78 g (80%).

Mp 196–197 °C (sublimed) (Lit. 197 °C,[19a] 187–192 °C[19b]).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.00 (s, 1 H), 8.55 (dd, 1 H, *J* = 1.3, 4.9 Hz), 8.15 (d, 1 H, *J* = 7.9 Hz), 7.99 (s, 1 H), 7.40 (dd, 1 H, *J* = 4.7, 7.6 Hz).

MS (CI, NH_3): *m*/*z* = 147 [M + H$^+$].

5-(2-Nitro-1-phenylethyl)-4-phenyl-1*H*-1,2,3-triazole (9a)

If, instead of adding the nitrostyrene slowly to the NaN_3, as above, the components were simply dissolved in DMSO and heated according to the typical procedure used for the triazoles in Figure 1, the reaction led not only to triazole **2a**, but also to 1,3,5-triphenylbenzene (**3a**) and triazole **9a**. The latter compound was isolated as a solid after chromatography (silica gel, toluene–EtOAc 8:2).

Yield: 0.118 g (40%).

Mp 138–140 °C (Et_2O–PE).

IR (CCl_4): 3450, 3162 (NH), 1557 cm^{-1} (NO_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (m, 10 H, C*H*Ar), 5.26 (dd, 1 H, *J* = 8.9, 13.2 Hz), 5.13 (dd, 1 H, *J* = 6.7, 8.9 Hz), 4.90 (dd, 1 H, *J* = 6.6, 13.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 137.4 (*C*q), 129.3, 129.0, 128.9, 128.2, 128.0 (*C*H), 79.0 (*C*H_2), 40.5 (*C*H).

MS (CI, NH_3): *m*/*z* = 295 [M + H$^+$], 312 [M + H$^+$ + NH_3].

HMRS (EI): [M$^+$] calcd for $C_{16}H_{14}N_4O_2$: 294.1116; found: 294.1128.

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